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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
06/05/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/557,602	KON ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2009 and 22 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24,26-28,40 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24,26-28,40 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/23/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 3/23/09 and 4/22/09, is acknowledged.

2. Claims 24, 26-28, 40 and 41 are pending and under examination in the instant application.

3. Applicant's IDS, filed 3/23/09, is acknowledged.

4. In view of the amendment filed on 3/23/09 and 4/22/09, only the following rejections are remained.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 40 stands rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treatment of autoimmune hepatitis with anti-RGDSVVYGLR antibodies, does not reasonably provide enablement for a method for treatment of diseases caused by activation of imunocompetent cells, comprising administering to a patient in need thereof a therapeutic agent comprising, as the active ingredient, an immunocompetent cell activation inhibitor comprising an antibody to osteopontin or a peptide fragment thereof claimed in claim 40. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action mailed 11/21/09.

Applicant's arguments, filed 3/23/09 and 4/22/09, have been fully considered, but have not been found convincing.

Based on Applicant admission on page 6, 3rd-7th paragraphs of the remarks, that it is common knowledge in the field that "general therapeutics for autoimmune diseases are not effective for treating hepatitis". Applicant has provided four references (Nat. Clin Pract Gastroenterol Hepatol, 2007, 4(4):202-214, Dig Dis Sci, 2008, Am J. Gastroenterol 1999, 94(1):241-8, Can J Gastroenterol, 2008, 22(4):388-92) to show that the ineffectiveness of general therapy for treating hepatitis are not effective. In the absence of evidence that the claimed anti-OPN antibody would be effective in treating viral hepatitis or drug-induced hepatitis, the rejection is maintained.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 24, 26-28 and 41 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/63241 for the same reasons set forth in the previous Office Action mailed 11/21/09.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/63241 as applied to claims 24-39 and 41-42 above, and further in view of Authur (Autoimmune Liver Disease, 53-56, 2002) for the same reasons set forth in the previous Office Action mailed 11/21/09.

Applicant's arguments, filed 3/23/09 and 4/22/09, have been fully considered, but have not been found convincing.

Applicant submits that the WO `241 publication describes modulating immune responses generally using modulators of ETA-1, also known as osteopontin. The WO`241 publication generally describes modulating an immune response using modulators of ETA-1 which inclusive of antibodies that block or neutralize the interaction of ETA-1 with a cell surface receptor. However, Applicant argues that while the `241 publication generally describes the treatment of immune related disease, the `241 does not fairly suggest that hepatitis specifically could be treated wit antibodies directed to the specific amino acid sequences claimed here.

Contrary to applicant assertions, the `241 publication teaches a method for modulating immune responses in a subject using modulators of ETA-1/osteopontin. Further the `241 publication teaches methods of treating autoimmune disorder such as chronic active hepatitis (see page 53, lines 10-27 in particular), wherein the Eta-1/osteopontin modulator is an antibody which

specifically binds Eta-1/osteopontin (see published claim 42), wherein the antibody is specific for the RGD sequence of Eta-1/osteopon (e.g., the integrin binding domain) (see page 32, lines 12-14). The `241 publication teaches VVYGLR as N-terminal fragment containing the RGD motif (see page 70, lines 6-10).

Applicant further argues that it is common knowledge in the field that general therapeutics for autoimmune diseases are not effective for treating hepatitis. Applicant points to Nat. Clin Pract Gastroenterol Hepatol, 2007, 4(4):202-214, Dig Dis Sci, 2008, Am J. Gastroenterol 1999, 94(1):241-8, Can J Gastroenterol, 2008, 22(4):388-92. Applicant points also to the enablement rejection in the previous Office Action, mailed 11/21/08 to support the contention that the `241 publication yields only one conclusion, the `241 does not enable the treatment of hepatitis. In order for a reference to anticipate a claimed invention, the reference or references must provide an enabling disclosure sufficient to place the public in possession of the claimed invention. Likewise, this analysis extends to obviousness, where a holding of obviousness cannot be sustained "unless there is some known or obvious way to make the thing or to carry out the process."

However, with respect to the obviousness rejection of claim 40, it is noted that while Applicant's arguments mounts to a double standard because applicants accepting their specification to enable for the viral hepatitis or drug-induced hepatitis, yet contends that the prior art under obviousness is not enabled. It is noted that the Examiner enabled only the autoimmune hepatitis. Applicant cannot represent to the public that their claimed method can treat viral hepatitis or drug-induced hepatitis using specific underlying logic, while at the same time discounting the relevance of that very same logic to the obviousness of their claims. Applicant has not demonstrated efficacy on viral- or drug-induced hepatitis. If the specification is enabled, so is the prior art and vise versa.

With respect to the anticipatory rejection, it is noted that the standard for what constitutes proper enablement of a prior art reference for purposes of anticipation under Section 102 differs from the enablement standard under Section 112 because section 112 provides that the specification must enable one skilled in the art to "use" the invention whereas Section 102 makes no such requirements as to an anticipatory disclosure. See *In re Hafner*, 410 F.2d at 1404.

"The reason is that section 112 "provides that the specification must enable one skilled in the art to 'use' the invention whereas [section] 102 makes no such requirement as to an anticipatory disclosure." *Hafner*, 410 F.2d at 1405; *see 1* Donald S. Chisum, *Chisum on Patents* § 3.04[1][c] (2002); *see also In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1349-52 (Fed.Cir.2002) (finding anticipation where applicant sought a patent based on a new use for a previously disclosed method)."

11. The following new ground of rejections are necessitated by the amendment submitted 4/22/09.

12. Claims 24, 26-28 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/63241 (of record) in view of WO 02/081522 (IDS reference).

The `241 publication teaches a method for modulating immune responses in a subject using modulators of Eta-l (early T lymphocyte activation-l)/ostcopontin. The `241 publication teaches methods of treating infections, immune disorders and diseases, autoimmune disorders and diseases, various immunodeficiencies and cancer (see abstract), wherein the autoimmune disorder is chronic active hepatitis (see page53, lines 10-27). The `241 publication claims A method of modulating a type-1 immune response in a subject comprising administering to said subject an Eta-1/osteopontin modulator such that the type-1 immune response is modulated (published claim 1). A method of downregulating a type-1 immune response in a patient comprising: (a) selecting a patient suffering from a disorder that would benefit from a downregulated type-1 immune response: and (b) administering to said patient an Eta-1/osteopontin inhibitory modulator such that the type-1 immune response is downregulated (see published claim 11), wherein the disorder is selected from the group consisting of bacterial arthritis, granulomatous disorder, glomerulonephritis, rheumatoid arthritis, multiple sclerosis, herpes simplex keratitis, and autoimmune disease (diseases caused by activation of immunocompetent cells) (see published claim 12), wherein said Eta-1/osteopontin modulator is an antibody which specifically binds Eta-1/osteopontin (see published claim 42), wherein the antibody is specific for the *RGD sequence* of Eta-1/osteopontin (e. g., the integrin binding domain) (page 32, line 12-14). The `241 publication teaches that the immune cell being modulated are a macrophage, a dendritic cell, a T cell, a B cell, a monocyte and a neutrophil (immunocompetent cells) (see published claim 20). The publication teaches VVYGLR (e. g., amino acid residues 162-168 of SEQ ID NO : 2), an N-terminal fragment ("Eta-1/opn NT) containing the RGD motif (see page 70, lines 6-10).

The `241 publication teachings differs from the claimed invention only in the recitation that the antibody can inhibit binding between an integrin recognizing the amino acid sequence SVVYGLR and osteoponin or a peptide fragment thereof, in claim 24.

However, the `522 publication teaches the use of an anti-osteopontin antibody to inhibit the binding of an integrin to osteopontin which inhibits the binding of the integrin recognizing RGD sequence to osteopontin and recognizes SVVYGLR sequence. The `522 publication teaches that the antibody is useful for remedies for autoimmune diseases, rheumatism, rheumatoid arthritis or arthritis deformans containing any of the anti-osteopontin antibodies as active ingredient (see abstract in particular).

It would have been obvious at the time the invention was made to substitute the anti-OPN antibodies taught by the `241 publication with the anti-osteopontin antibody to inhibit the binding of an integrin to osteopontin which inhibits the binding of the integrin recognizing RGD sequence to osteopontin and recognizes SVVYGLR sequence taught by the `522 publication.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because both prior art antibodies inhibits the binding of an integrin to osteopontin through the RGD N-terminal fragment containing the VVYGLR sequence.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. Claims 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/63241 in view of WO 02/081522 (IDS reference), as applied to claims 24, 26-28 and 41 above, and further in view of Authur (Autoimmune Liver Disease, 53-56, 2002).

The teachings of the `522 and `241 publication have been discussed, supra.

The reference teachings differ from the claimed invention only in the recitation of viral hepatitis.

Arthur teaches that autoimmune hepatitis can present as an acute illness resembling severe acute viral hepatitis (see page 56, under practice points in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the autoimmune hepatitis disease taught by the `241 publication for the viral hepatitis disease taught by Arthur in a treatment method using anti-OPN antibody.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because autoimmune hepatitis present as an acute illness resembling severe acute viral hepatitis as taught by Arthur.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. In view of Applicant's amendment to recite "treating hepatitis" the previous rejection on the ground of nonstatutory obviousness-type double patenting over copending Application No. 11/836,078 or 11/755,671, is hereby withdrawn.

15. No claim is allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

June 2, 2009

/Maher M. Haddad/
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